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Age at menarche, total mortality and mortality from ischaemic heart disease and stroke: the Adventist Health Study, 1976–88

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Background Little is known about the relationship between age at menarche and total mortality and mortality from ischaemic heart disease and stroke.

Methods A cohort study of 19 462 Californian Seventh-Day Adventist women followed-up from 1976 to 1988. A total of 3313 deaths occurred during follow-up, of which 809 were due to ischaemic heart disease and 378 due to stroke.

Results An early menarche was associated with increased total mortality (*P*-value for linear trend <0.001), ischaemic heart disease (*P*-value for linear trend = 0.01) and stroke (*P*-value for linear trend = 0.02) mortality. There were, however, also some indications of an increased ischaemic heart disease mortality in women aged 16–18 at menarche (5% of the women). When assessed as a linear relationship, a 1-year delay in menarche was associated with 4.5% (95% CI 2.3–6.7) lower total mortality. The association was stronger for ischaemic heart disease [6.0% (95% CI 1.2–10.6)] and stroke [8.6% (95% CI 1.6–15.1)] mortality.

Conclusions The results suggest that there is a linear, inverse relationship between age at menarche and total mortality as well as with ischaemic heart disease and stroke mortality.

Keywords Myocardial infarction, menarche, mortality, stroke

Introduction

The menarche is a very important event in the life of a woman. The impact of age at menarche on later morbidity has, however, received little attention except for the association with breast cancer risk.[1] Recently, it was found that an early menarche may increase total mortality.[2] Thus, hormonal changes early in life have impact on health many decades later.

Results from previous studies regarding relationships between age at menarche and stroke,[3–5] and ischaemic heart disease[3,6–9] morbidity have been inconclusive. However, results from both case-control and prospective studies may be confounded.

In the present study, we investigate associations between age at menarche and total mortality as well as deaths due to ischaemic heart disease and stroke in a population with extensive information about many possible confounders, in particular life style. We were, for example, able to analyse these relationships in a large group of women who never had smoked. Our hypothesis is that age at menarche is inversely related

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to total mortality, ischaemic heart disease and stroke mortality.

Material and methods

In 1974, a census questionnaire was mailed to the head of all identified Seventh-Day Adventist households in California. Sixty percent of the households returned this questionnaire. Two years later, 75% of the white, non-Hispanic Seventh-Day Adventists aged 25 years and older who had previously had been identified by the Census Questionnaire returned a new postal questionnaire (the Lifestyle Questionnaire).[10,11]

The Lifestyle Questionnaire included question concerning age at menarche ('As nearly as you can recall, about how old were you when you had your first menstrual period'). We identified 19 462 women with a plausible age at menarche between the age of 9 and 18 (thereby excluding 17 and 13 women who reported menarche <9 and >18 years, respectively). This represents 99% of the women who returned the Lifestyle Questionnaire.

Age at menarche was initially categorized into <11, 11, 12, 13, 14, 15, 16 and >16 years. The reference group was women who were aged 13 years at menarche. In the analyses for ischaemic heart disease and stroke mortality, the two top and bottom two categories have been merged.

Associations between age at menarche and some possible confounders were adjusted for age by analysis of covariance. Information about these variables was obtained from the Lifestyle Questionnaires. This included questions about a large number of other topics like aspects of reproduction (e.g. parity, age at menopause, type menopause, past and current use of oral contraceptives and hormone replacement therapy), dietary habits (both current and previous), self-reported weight and height, smoking and alcohol, physical activity and level of education. Body mass index was computed as kg/m^2. The possible confounders were categorized as shown in Table 1. Relationships between age at menarche and mortality were investigated in proportional hazard regression models using attained age as the continuous time variable. The proportional hazard assumption is that the relative hazard rates associated with the age at menarche are constant across different age groups. This assumption was tested by checking the statistical significance of the product term between age at menopause and attained age.

In the main analyses, displayed in the tables, the different ages at menarche were entered into the model as dummy variables. In the analyses where the effects of possible confounders were assessed, age at menarche was included in the model as a continuous variable with eight (for total mortality) or six (for ischaemic heart disease and stroke mortality) levels as described above and shown in the tables. This was in order to assess the effects of adjustments on the possible linear relationship between age at menarche and mortality. The possible confounders included in the model were categorized as shown in Table 1. Due to missing values, the number of women included in the analyses may change somewhat from one analysis to the next. There are relatively few women with missing values for most of the variables included in the analyses. Information about smoking, physical activity in leisure, parity and, at first birth (in women with children) and menstrual status was missing for $\leqslant 2\%$ of the women, about type of menopause or use of hormone replacement therapy for 3–4% in post-menopausal women. Data concerning current use of meat or the use of oral contraceptives were missing for 6% of the women. The largest percentages of missing values were found for information about body mass index (10%), educational level (16%) and childhood vegetarian status (22%).

The follow-up started when the Lifestyle Questionnaire was returned and ended when the respondent died or on December 31, 1988. Follow-up was achieved by computerized matching to the California state death tapes and to the National Death Index, supplemented by church records and information from the families of the respondents. Validity studies suggest that at most 3–4% of deaths have been missed.[10] Death certificates were obtained and the ICD-9 code for underlying cause of death was assigned by an experienced nosologist. Any one of codes 410–414 and 430–438 was used as the definition of ischaemic heart disease and stroke, respectively. Analyses were performed using SAS Software.[12]

Results

The mean (SD) and median ages at menarche in the women included in our analysis were 12.8 (1.5) and 13 years, respectively. The mean age at start of follow-up was 55.1 years (range: 26–101) and the mean follow-up period was 11.1 years (range: 0–12 years).

Relationships between age at menarche and demographic and lifestyle variables

We found that the age at menarche was higher in women who were relatively old at enrolment (Table 1). In age-adjusted analyses, there was no relationship ($P = 0.15$) between smoking and age at menarche. High levels of education or body mass index at enrolment were associated with a relatively low age at menarche (both $P < 0.001$), whereas high physical activity was related to a higher age at menarche ($P = 0.003$). Current meat consumption, a childhood vegetarian diet and parity were not correlated to age at menarche ($P = 0.52$, 0.48 and 0.40, respectively); whereas age at first birth was positively associated with age at menarche ($P < 0.001$). Women with hysterectomy reported

Table 1 Age-adjusted relationships between some demographic and life style variables and age at menarche at baseline in 1976 in 19462 Californian Seventh-Day Adventist women included in a 12-year mortality follow-up

	Number of women (%)	Mean age at menarche
Age at entry (years)		
25–39	4674 (24.0)	12.37
40–54	4897 (25.2)	12.65
55–69	5698 (29.3)	13.02
70+	4193 (21.5)	13.36
***P*-value for linear trend**		<0.001
Smoking status		
Current smoker	376 (2.0)	12.94
Past smoker	2579 (13.5)	12.80
Never smoked	16146 (84.5)	12.84
***P*-value**		0.15
Years of education (years)		
<9	1737 (10.6)	12.94
9–11	2354 (14.4)	12.83
12	5176 (31.6)	12.82
13–15	3877 (23.7)	12.74
16	2316 (14.1)	12.74
>16	918 (5.6)	12.76
***P*-value for linear trend**		<0.001
Level of exercise		
No exercise	6636 (34.7)	12.80
Some exercise	2267 (11.9)	12.81
Low-level exercise	3251 (17.0)	12.83
High-level exercise	6949 (36.4)	12.89
***P*-value for linear trend**		0.003
BMI (Kg/m^2)		
<20	2293 (13.1)	13.12
20–24	9013 (51.3)	12.94
25–29	4246 (24.2)	12.66
30+	2008 (11.4)	12.41
***P*-value for linear trend**		<0.001
Current meat consumption (Per week)		
Never	5644 (30.9)	12.85
<1	4197 (23.0)	12.84
1–4	3842 (21.0)	12.84
>4	4591 (25.1)	12.82
***P*-value for linear trend**		0.52
Childhood vegetarianism		
No	13045 (86.6)	12.75
Yes	2018 (13.4)	12.75
***P*-value**		0.48
Parity (No. of children)		
None	3618 (19.0)	12.85
1	2930 (15.4)	12.85
2	5326 (28.0)	12.84
3	3669 (19.3)	12.82
4	1966 (10.3)	12.83
>4	1538 (8.1)	12.83
***P*-value for linear trend**		0.40
Age at first delivery (years)		
<19	1584 (10.3)	12.52
19–20	2798 (18.2)	12.81
21–22	2988 (19.5)	12.85
23–24	2617 (17.1)	12.87
25–28	3324 (21.6)	12.89
>28	2042 (13.3)	12.95
***P*-value for linear trend**		<0.001
Oral contraceptives		
Never taken	12902 (70.3)	12.84
Current/past user	5457 (29.7)	12.80
***P*-value**		0.19
Menstrual status		
Currently pregnant	399 (2.1)	13.01
Regular cycle	5186 (27.1)	12.86
Irregular cycle	1115 (5.8)	12.90
Menopause	12405 (64.9)	12.81
***P*-value**		0.04
Type of menopause		
Hysterectomy	5454 (45.3)	12.91
Normal	6254 (51.9)	13.10
Other	338 (2.8)	13.05
***P*-value**		<0.001
Hormone replacement therapy		
Never taken	5057 (42.4)	13.07
Current/past user	6870 (57.9)	12.97
***P*-value**		<0.001

The Adventist Health Study, 1976–1988. Results are adjusted for age at enrolment.

lower age at menarche than other post-menopausal women ($P < 0.001$). Women who had used hormone replacement therapy had a somewhat lower age at menarche than never users ($P < 0.001$), but there was no association with use of oral contraceptives ($P = 0.19$). However, except for the association with

Table 2 Total mortality according to age at menarche in a 12-year follow-up of 19 462 Californian Seventh-Day Adventist women

Age at menarche (years)	Number of women	Person-years	Deaths	MRR* (95% CI)
<11	872	9799	103	1.45 (1.18–1.78)
11	2522	28 338	351	1.20 (1.06–1.36)
12	4737	53 227	674	1.11 (1.01–1.23)
13	5588	62 398	863	1.00
14	3298	35 761	713	0.96 (0.87–1.06)
15	1419	15 306	336	0.96 (0.85–1.09)
16	772	8036	206	1.11 (0.96–1.30)
>16	254	2621	68	0.88 (0.69–1.13)
Mean percentage reduction in mortality[a]			4.5 (95% CI 2.3–6.7)	
P-value for linear trend			<0.001	

Results are adjusted for attained age.
The Adventist Health Study, 1976–1988.
[a]The mean percentage of reduction in mortality associated with a category higher menarche age group (95% CI).
MRR, mortality rate ratio.

age at entry (i.e. birth cohort) and body mass index, the associations between age at menarche and the demographic and life style variables considered were relatively weak.

Total mortality

A total of 3313 deaths occurred during follow-up; 809 from ischaemic heart disease and 378 deaths from stroke. The mean age at death was 80.8 years. Relationships between age at menarche and total mortality are displayed in Table 2 and demonstrate a linear, inverse relationship ($P < 0.001$). Comparing women with early (aged 9 or 10) vs late (aged 17 or 18) menarche, the latter had an ~40% (95% CI 18–55) lower total mortality. In a model where age at menarche was included in the model as a continuous variable with scores 1–8 (reflecting the eight different ages at menarche in Table 2), one level increase in menarcheal age category was associated with a mean 4.5% (95% CI 2.3–6.7) lower mortality. The relationship between age at menarche and total mortality did not depend on attained age. Additional adjustment for birth cohort or exclusion of women aged 9 and 18 at menarche, did not influence the association presented in Table 2.

The relationship between age at menarche and total mortality was found only in post-menopausal women (*P*-value for interaction = 0.04). In these women one level increase in menarcheal age category was associated with a mean 4.9% (95% CI 2.6–7.2) lower mortality. As 93% of the deaths were among post-menopausal women, the results essentially reflect the relationships between age at menarche and total mortality in this group of women.

We also performed analyses stratified for smoking habits. Only 16% of the women had ever smoked cigarettes; 2% were current smokers. There were indications of a stronger association between age at menarche and total mortality in women who ever had smoked [one category higher menarcheal age group was associated with a mean 9.4% (95% CI 3.3–15.2) lower mortality] than in never smokers [3.9% (95% CI 1.4–6.3) *P*-value for interaction = 0.06].

In separate analyses, we adjusted for a number of possible confounders, including only one of these variables at a time in the model. These variables were birth cohort, educational level, physical activity, childhood vegetarianism, current meat consumption, parity, age at first birth of a living child, body mass index and smoking (never, ex-smoker and current smoker). None of these adjustments influenced materially the inverse relationship between age at menarche and total mortality with a 3–5% reduction in total mortality associated with one category higher menarcheal age group. Furthermore, the results were essentially unaffected by adjustment for use of oral contraceptives, menopausal status, type of menopause and use of hormone replacement therapy in post-menopausal women.

Mainly because of the interaction with menstrual status (the association was found only in post-menopausal women) and the inverse relationship between age at menarche and age at first birth, we performed a separate set of analyses restricted to post-menopausal women with information about body mass index, physical activity, age at first birth, type of menopause and use of hormone replacement therapy, i.e. 8262 women with 1757 deaths. The main reason for the lower number of women included in this analysis compared with the analysis with all women (19 462 women) was that it was restricted to post-menopausal, parous women, i.e. 9771 women. Furthermore, information about body mass index was missing for 9% of these women. In this subpopulation, *P*-value for the age-adjusted association with age

Table 3 Ischaemic heart disease and stroke mortality according to age at menarche in a 12-year follow-up of 19 462 Californian Seventh-Day Adventist women

			Ischaemic heart disease		Stroke	
Age at menarche (years)	Number of women	Person-years	Deaths	MRR (95% CI)	Deaths	MRR (95% CI)
<12	3394	38 137	111	1.37 (1.09–1.73)	52	1.43 (1.02–2.01)
12	4737	53 227	166	1.20 (0.98–1.48)	74	1.17 (0.86–1.59)
13	5588	62 398	203	1.00	93	1.00
14	3298	35 761	171	0.93 (0.76–1.14)	99	1.14 (0.86–1.52)
15	1419	15 306	83	0.95 (0.74–1.23)	32	0.78 (0.52–1.17)
>15	1026	10 656	75	1.14 (0.88–1.49)	28	0.90 (0.59–1.37)
Mean percentage of reduction in mortality[a]			6.0 (95% CI 1.2–10.6)		8.6 (95% CI 1.6–15.1)	
P-value for linear trend			0.01		0.02	

Results are adjusted for attained age.
The Adventist Health Study, 1976–1988.
[a]The mean percentage of reduction in mortality associated with a category higher menarche age group (95% CI).
MRR, mortality rate ratio.

at menarche was 0.05. One category higher menarcheal age group was associated with a mean 3.2% lower mortality analyses. Adjustment for these variables reduced the strength of the association to 2.3% ($P = 0.15$).

Ischaemic heart disease mortality

Table 3 gives the results for the relationships between age at menarche and ischaemic heart disease mortality. One category higher menarcheal age was associated with a mean 6.0% (95% CI 1.2–10.6) lower mortality ($P = 0.01$). We did note, however, a relatively high mortality in women who were >15 years at menarche, i.e. 5% of the women. A second order term was statistically significant ($P = 0.005$), suggesting a U-shaped relationship between age at menarche and ischaemic heart disease mortality. This U-formed shape of the relationship was also found if women with early (age 9) and late (age 18) menarche or women who reported diabetes at enrolment were excluded from our analyses. We did not find any indication of an interaction with attained age.

We found no interactions by menopausal status or use of hormone replacement therapy (never/ever) ($P = 0.6$ in both cases). In women who had ever smoked cigarettes, one category higher menarcheal age group was associated with a mean 17.6% (95% CI 3.8–29.4) lower mortality. In never smokers, the corresponding figure was 5.2% (95% CI: −0.1 to 10.2). The relationship in ever smokers was based on 83 deaths only, however, and the *P*-value for interaction was 0.07.

Similarly as for the analyses for total mortality, we adjusted for birth cohort and a number of other possible confounders as outlined above for analyses of total mortality. The strength of the linear relationship was in some situations reduced by these adjustments. In analyses restricted to parous women with a known age at first delivery the *P*-value was 0.13. Before adjustments, one category higher menarcheal age was associated with 4.4% (95% CI −1.3 to 9.8) lower mortality. After adjustments, one category higher menarcheal age was associated with 3.4% (95% CI −2.4 to 8.9) lower mortality and the *P*-value was 0.25. In analyses restricted to postmenopausal women with data about body mass index, physical activity, age at first delivery, type of menopause and hormone replacement therapy, the *P*-value for the relationship was both before and after adjustment for these possible confounders 0.3. Before adjustments, one category higher menarcheal age was associated with 3.5% (95% CI −3.4 to 9.1) lower mortality. After adjustments, one category higher menarcheal age was associated with 1.7% (95% CI −5.2 to 8.3) lower mortality. Thus, some degree of confounding by these variables was present.

Stroke mortality

The results for stroke mortality are also displayed in Table 3. One category higher menarcheal age was associated with a mean 8.6% (95% CI 1.6–15.1) lower stroke mortality and the relationship was linear. There was no indication of an interaction with attained age. Exclusion of women aged 9 and 18 at menarche from the analyses did not influence our findings. No interactions were found for menopausal status, smoking or use of hormone replacement therapy (both categorized into never or ever smoking or use of hormones, respectively) (all *P*-values >0.4). One category higher menarcheal age was associated with 7.8% (95% CI 0.3–14.7) lower stroke mortality in women who never had smoked cigarettes.

Adjustments for the same possible confounders introduced in the model one at the time, revealed no important confounding. The multivariate adjustments confirmed this picture. In the analysis adjusted

for body mass index, physical activity, age at first delivery, type of menopause and use of hormone replacement therapy in post-menopausal women, the *P*-value for the relationship was 0.06 both before and after adjustment for these possible confounders. Before adjustments, one category higher menarcheal age was associated with 9.4% (95% CI −0.6 to 18.6) lower mortality. After adjustments, one category higher menarcheal age was associated with 9.6% (95% CI −0.4 to 18.6) lower mortality.

Discussion

In this study of the relationship between age at menarche and total mortality as well as mortality from ischaemic heart disease and stroke, we find inverse age-adjusted relationships that are partially explained by associations between age at menarche and other variables. The associations seem stronger and more convincing for stroke mortality than for deaths caused by ischaemic heart disease.

The results from this study confirm the results from a large Norwegian study as they also found an inverse relationship with total mortality.[2] We do not, however, find an interaction with attained age, whereas the inverse relationship was found to be stronger in relatively young (aged <70 years) women in the Norwegian study.[2] The reason for this discrepancy is not obvious. To our knowledge, there are no other studies to compare with. The inverse relationship with total mortality could not be explained by deaths due to breast cancer as only 137 out of 3313 (4%) of deaths were attributed to breast cancer (results not shown).

Our results indicate that an early menarche may increase the risk of ischaemic heart disease. A previous prospective study with 308 cases of myocardial infarction reported a non-significant ($P = 0.2$) inverse relationship between age at menarche and ischaemic heart disease[6] and a study with a total of 45 cases found an inverse association.[7] In other studies,[3,8,9] including the largest one, a case-control study with 839 cases,[8] no association was found.

We base our analyses on the cause of death stated on the death certificates. As is common in most studies relying on death certificates only, most strokes were classified as ill-defined cerebrovascular, but it is known from autopsy studies that the majority of the strokes in Western countries are ischaemic strokes. Early menarche (<13 years old) increased the risk of ischaemic strokes in a case-control study with 430 cases.[5] This is in accordance with our results. However, others have found increased stroke mortality in women with late menarche (aged >16) in a cohort study where a relatively large proportion of the 487 stroke deaths included were haemorrhages.[3] A strong inverse relationship between age at menarche and haemorrhagic stroke risk was found in a Korean case-control study with 197 cases.[4]

The reproducibility[13–15] and validity[16,17] of data on age at menarche has in previous studies been found to be acceptable. A total of 3103 Adventist women from this study also enrolled in a new cohort study 25 years later where they reported their age at menarche in a new survey (Adventist Health Study-2 conducted in 2002–06). We found a correlation coefficient of 0.85 between age at menarche reported in the two studies (Keiji Oda, unpublished data).

The women included in the present study are probably not representative of all Californian Seventh-Day Adventist women, and even less of women at large. However, for our purpose; to study the relationship between age at menarche and mortality, the distribution of age at menarche is of minor importance and the large proportion of never smokers is an advantage. A relatively high adolescent body weight increases the likelihood of early menarche.[18–21] No data were available concerning body weight during childhood or adolescence among women included in this cohort, and the adult height and weight were self-reported. The reproducibility of data about self-reported weight in this cohort has been found to be very high as the correlation between the weight reported on in questionnaire and the weight measured up to 1 year later was 0.95.[22] However, the weight reported may still be biased, and probably more in subjects with low menarcheal age as they had the highest weight as adults and body mass index measured at one point in time is strongly correlated to body mass index measured many years later.[23,24] Many studies have, like we have, demonstrated an inverse relationship between age at menarche and body mass in adulthood,[25] but the explanation to this finding, according to new studies, may be the relationship between premenarcheal weight and age at menarche.[18] Anyhow, as a high body mass index increases mortality, [26,27] body mass index could be a relevant confounder, but adjustment for body mass index when assessing the relationships between age at menarche and mortality did not influence the relationship.

Food habits during childhood and adolescence, even after adjusting for body size, may influence age at menarche and girls who are vegetarians may get their first period later in life than other girls.[28] This may be relevant for the findings in our study because vegetarianism is much more common in this population of Seventh-Day Adventists (31% of the included women reported at enrolment that they never eat meat) than in the general population. However, a recent study found no difference in age at menarche between lifelong vegetarian women and women who became vegetarians at age 20 or older.[29] We did not find any difference in menarcheal age between women who had been vegetarians during childhood and other women (Table 1), and adjustment for this variable (or whether the parents were vegetarians or not) did not influence our results.

Physical activity is associated with delayed menarche[30–32] and reduced mortality. No data were available about the level of physical activity of the women during childhood or adolescence, but a positive relationship between age at menarche and physical activity in 1976 was found at enrolment (Table 1). Adjustment for this variable did not, however, influence the relationship investigated.

Recent studies show that girls with an early menarche tend to smoke as teenagers,[33] but we do not know whether this effect of age at menarche on smoking prevalence applies to this cohort where the majority of the women have been socialized into the Adventist Church which strongly discourages smoking. An inverse relationship between age at menarche and smoking prevalence could theoretically have explained the higher mortality in women with an early menarche. However, adjustments for smoking (current, previous or never smoker) did not influence our results. Importantly, the relationships were statistically significant also when the analyses were restricted to women who had never smoked (*P*-value for linear trend = 0.002, 0.05 and 0.04 for total, ischaemic heart disease and stroke mortality, respectively).

Unfortunately, we have no information about some important risk factors for cardiovascular diseases like measured blood lipids or blood pressure. Early menarche has in some studies been found to be associated with increased cardiovascular risk factor levels in young women.[34] There are also indications that age at menarche is associated with metabolic risk factors for cardiovascular diseases in middle-aged women.[25] However, it is debatable to what extent it is correct to adjust for variables that may be part of the causal path between low age at menarche and increased mortality.

We have in our analyses adjusted for a number of possible confounders, and analyses stratified by smoking demonstrate that our results cannot be explained by this important possible confounder. However, particularly for ischaemic heart disease, the adjustments for considered confounders seem to have some impact on our results. Furthermore, residual confounding by measured or unmeasured variables cannot, of course, be ruled out.

An extreme age at menarche may reflect medical conditions which can influence mortality. Nutritional deficiencies associated with chronic illness (e.g. inflammatory bowel disease), general malnutrition, anorexia nervosa and diabetes may delay menarche,[35,36] but this cannot explain our main finding of inverse relationships. Furthermore, exclusion of women in our cohort with very early (aged 9 years) and late (aged 18 years) menarche only slightly influenced the relationship between menarcheal age and mortality.

For ischaemic heart disease mortality, we found an increased risk in women aged 16–18 at menarche, i.e. 5% of the women in this cohort. We have no obvious explanation for this. The most prevalent relevant chronic disease that we have information about is diabetes mellitus. However, exclusion of all women who reported diabetes at enrolment (some of them may have had diabetes before menarche) did not explain the increased risk in women with a very late menarche.

Recent data suggest that a late menarche may reduce the diabetes risk as adults.[37] Diabetes is an established risk factor for cardiovascular diseases.[38] Thus, the inverse relationship between age at menarche and diabetes risk may partly explain an inverse relationship between age at menarche and cardiovascular risk.

In summary, we find that women with an early menarche have a moderately increased total, ischaemic heart disease and stroke mortality. This study included more than 3000 deaths in total, and more than 800 and 370 deaths due to ischaemic heart disease and stroke, respectively. Even so, there is a need for studies including significantly larger number of cases in order to reduce the width of the confidence intervals and get a more precise picture of how age at menarche influences ischaemic heart disease and stroke mortality.

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Conflict of interest: None declared.

KEY MESSAGES

- Age at menarche is inversely related to total mortality.
- One year delay in menarche was associated with 4.5% (95% CI 2.3–6.7) lower total mortality.
- Similar results was found for ischaemic heart disease and stroke mortality.

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